

24 6/7/1-2

6/7/1 (Item 1 from file: 399)

110129853 CA: 110(15)122858a JOURNAL

Deletions screening of the Duchenne muscular dystrophy locus via multiplex DNA amplification

AUTHOR(S): Chamberlain, Jeffrey S.; Gibbs, Richard A.; Ranier, Joel E.;

Nguyen Phi Nga; Caskey, C. Thomas

LOCATION: Inst. Mol. Genet., Baylor Coll. Med., Houston, TX, 77030, USA

JOURNAL: Nucleic Acids Res. DATE: 1988 VOLUME: 16 NUMBER: 23 PAGES:

11141-54 CODEN: NARHAD ISSN: 0305-1048 LANGUAGE: English

SECTION:

CA203005 Biochemical Genetics

CA213XXX Mammalian Biochemistry

CA214XXX Mammalian Pathological Biochemistry

IDENTIFIERS: Duchenne muscular dystrophy deletion mutation screening, human Duchenne muscular dystrophy diagnosis, DNA multiplex amplification gene deletion screening

DESCRIPTORS:

Deoxyribonucleic acid...

 multiplex amplification of, in screening for Duchenne muscular dystrophy gene deletions, in human

Gene and Genetic element, animal...

 For Duchenne muscular dystrophy, of human, rapid screening method for deletions in, multiplex DNA amplification in

 Muscular dystrophy, Duchenne...

 of, of human, rapid screening method for deletions in, multiplex DNA amplification in

Mutation, deletion...

 in Duchenne muscular dystrophy gene, of human, screening method for, multiplex DNA amplification in

Deoxyribonucleic acid sequences...

 of Duchenne muscular dystrophy gene deletion-prone exons and flanking introns, of human

6/7/2 (Item 2 from file: 399)

108162604 CA: 108(19)162604a JOURNAL

Expression of the murine Duchenne muscular dystrophy gene in muscle and brain

AUTHOR(S): Chamberlain, Jeffrey S.; Pearlman, Joel A.; Muzny, Donna M.; Gibbs, Richard A.; Ranier, Joel E.; Reeves, Alice A.; Caskey, C. Thomas

LOCATION: Inst. Mol. Genet., Baylor Coll. Med., Houston, TX, 77030, USA

JOURNAL: Science (Washington, D. C., 1883-) DATE: 1988 VOLUME: 239

NUMBER: 4846 PAGES: 1416-18 CODEN: SCIEAS ISSN: 0036-8075 LANGUAGE:

English

SECTION:

CA203003 Biochemical Genetics

CA213XXX Mammalian Biochemistry

CA214XXX Mammalian Pathological Biochemistry

IDENTIFIERS: Duchenne muscular dystrophy gene muscle brain, mRNA Duchenne muscular dystrophy mouse

DESCRIPTORS:

Brain, animal's... Muscle, metabolism...

 Duchenne muscular dystrophy gene expression, of mouse, mental retardation of human in relation to

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Duchenne muscular dystrophy gene of, expression in muscle and brain of, mental retardation in human in relation to

Ribonucleic acid formation, messenger...

Duchenne muscular dystrophy-related, in muscle and brain of mouse, mental retardation in human in relation to

Gene and Genetic element, animal, Dmd...

for Duchenne muscular dystrophy, expression of, in muscle and brain of mouse, mental retardation in human in relation to

Muscular dystrophy, Duchenne...

gene Dmd for, muscle and brain of mouse expression of, mental retardation in human in relation to

6/7/3 (Item 1 from file: 5)

0019124405 BIOSIS Number: 87059136

DELETION SCREENING OF THE DUCHENNE MUSCULAR DYSTROPHY LOCUS VIA MULTIPLEX

DNA AMPLIFICATION

CHAMBERLAIN J

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6/7/3 (Item 1 from file: 5)

0019124405 BIOSIS Number: 87059138

DELETION SCREENING OF THE DUCHENNE MUSCULAR DYSTROPHY LOCUS VIA MULTIPLEX

DNA AMPLIFICATION

CHAMBERLAIN J S; GIBBS R A; RANIER J E; NGUYEN P N; CASKEY C T

INST. MOLEC. GENET., BAYLOR COLL. MED., HOUSTON, TEX. 77030, USA.

NUCLEIC ACIDS RES 16 (23). 1988. 11141-11156. CODEN: NARHA

Language: ENGLISH

The application of recombinant DNA technology to prenatal diagnosis of many recessively inherited X-linked diseases is complicated by a high frequency of heterogenous, new mutations (1). Partial gene deletions account for more than 50% of Duchenne muscular dystrophy (DMD) lesions, and approximately one-third of all cases result from a new mutation (2-5). We report the isolation and DNA sequence of several deletion prone exons from the human DMD gene. We also describe a rapid method capable of detecting the majority of deletions in the DMD gene. This procedure utilizes simultaneous genomic DNA amplification of multiple widely separated sequences and should permit deletion scanning at any hemizygous locus. We demonstrate the application of this multiplex reaction for prenatal and postnatal diagnosis of DMD.

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6/7/4 (Item 2 from file: 5)

0019056570 BIOSIS Number: 36033667

RAPID DETECTION OF DELETIONS AT THE DUCHENNE MUSCULAR DYSTROPHY LOCUS VIA MULTIPLEX GENOMIC DNA AMPLIFICATION

CHAMBERLAIN J S; GIBBS R A; RANIER J E; NGUYEN P N; FARWELL N J; CASKEY C

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INST. MOLECULAR GENETICS, BAYLOR COLL. MED., HOUSTON, TEX.

32TH ANNUAL MEETING OF THE AMERICAN SOCIETY OF HUMAN GENETICS, NEW ORLEANS, LOUISIANA, USA, OCTOBER 12-15, 1988. AM J HUM GENET 43 (3 SUPPL.). 1988. A176. CODEN: AJHGAA

Language: ENGLISH

6/7/5 (Item 3 from file: 5)

0010595390 BIOSIS Number: 35050990

EXPRESSION OF THE MURINE DUCHENNE MUSCULAR DYSTROPHY GENE IN THE MUSCLE AND BRAIN OF NORMAL AND MUTANT MDX MICE
CHAMBERLAIN J S; PEARLMAN J A; GIBBS R A; RANIER J E; FARWELL N J; CASKEY C T
INST. MOLE. GENET., HOWARD HUGHES MED. INST., BAYLOR COLL. MED., HOUSTON, TX 77030, USA
MEETING ON CELLULAR AND MOLECULAR BIOLOGY OF MUSCLE DEVELOPMENT HELD AT THE UCLA (UNIVERSITY OF CALIFORNIA-LOS ANGELES) SYMPOSIUM ON MOLECULAR AND CELLULAR BIOLOGY, FEBRUARY 28-APRIL 10, 1988. J CELL BIOCHEM SUPPL 0 (12 PART C). 1988. 370. CODEN: JCBSD

Language: ENGLISH

6/7/4 (Item 4 from file: 5)

0018535020 BIOSIS Number: 35050613

EXPRESSION OF THE MURINE DUCHENNE MUSCULAR DYSTROPHY GENE IN THE MUSCLE AND BRAIN OF NORMAL AND MUTANT MDX MICE

CHAMBERLAIN J S; PEARLMAN J A; GIBBS R A; RANIER J E; FARWELL N J; CASKEY C T

INST. MOLE. GENET., HOWARD HUGHES MED. INST., BAYLOR COLL. MED., HOUSTON, TX 77030.

MEETING ON CELLULAR AND MOLECULAR BIOLOGY OF MUSCLE DEVELOPMENT HELD AT THE UCLA (UNIVERSITY OF CALIFORNIA-LOS ANGELES) SYMPOSIUM ON MOLECULAR AND CELLULAR BIOLOGY, FEBRUARY 28-APRIL 10, 1988. J CELL BIOCHEM SUPPL 0 (12 PART C). 1988. 319. CODEN: JCBSD

Language: ENGLISH

6/7/7 (Item 5 from file: 5)

0018253436 BIOSIS Number: 85121651

EXPRESSION OF THE MURINE DUCHENNE MUSCULAR DYSTROPHY GENE IN MUSCLE AND BRAIN

CHAMBERLAIN J S; PEARLMAN J A; MUZNY D M; GIBBS R A; RANIER J E; REEVES A A; CASKEY C T

INST. MOLECULAR GENETICS, BAYLOR COLL. MED., ONE BAYLOR PLAZA, HOUSTON, TX 77030.

SCIENCE (WASH D C) 239 (4846). 1988. 1416-1416. CODEN: SCIEA

Language: ENGLISH

Complementary DNA clones were isolated that represent the 5' terminal 2.5 kilobases of the murine Duchenne muscular dystrophy (Dmd) messenger RNA (mRNA). Mouse Dmd mRNA was detectable in skeletal and cardiac muscle and at a level approximately 90 percent lower in brain. Dmd mRNA is also present, but at much lower than normal levels, in both the muscle and brain of three different strains of dystrophic mdx mice. The identification of Dmd mRNA in brain raises the possibility of a relation between human Duchenne muscular dystrophy (DMD) gene expression and the mental retardation found in some DMD males. These results also provide evidence that the mdx mutations are allelic variants of mouse Dmd gene mutations.

6/7/8 (Item 1 from file: 155)

06781552 89063552

Deletion screening of the Duchenne muscular dystrophy locus via multiplex DNA amplification.

Chamberlain JS; Gibbs RA; Ranier JE; Nguyen PN; Caskey CT

Institute for Molecular Genetics, Baylor College of Medicine, Houston, TX 77030.

Nucleic Acids Res (ENGLAND) Dec 9 1988, 16 (23) p11141-56, ISSN 0305-1048 Journal Code: 08L

Language: ENGLISH

The application of recombinant DNA technology to prenatal diagnosis of many recessively inherited X-linked diseases is complicated by a high frequency of heterogeneous, new mutations (1). Partial gene deletions account for more than 50% of Duchenne muscular dystrophy (DMD) lesions, and approximately one-third of all cases result from a new mutation (2-5). We report the isolation and DNA sequence of several deletion prone exons from the human DMD gene. We also describe a rapid method capable of detecting the majority of deletions in the DMD gene. This procedure utilizes simultaneous cDNA amplification of multiple widely separated

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sequences and should permit deletion scanning at any hemizygous locus. We demonstrate the application of this multiplex reaction for prenatal and post natal diagnosis of DMD.

6/7/9 (Item 2 from file: 155)

04511022 83159232

Ex. analysis of the murine Duchenne muscular dystrophy gene in muscle and brain.

Shashidhar AG; Pearson JA; Muzny DM; Gibbs RA; Ranier JE; Caskey CT; Reeves AE

Institute for Molecular Genetics, Baylor College of Medicine, Houston, TX 77030.

Science Mar 18 1988, 239 (4846) p1416-8, ISSN 0036-8075

Journal Code: UJ7

Language: ENGLISH

Complementary DNA clones were isolated that represent the 5' terminal 2.5 kilobases of the murine Duchenne muscular dystrophy (Dmd) messenger RNA (mRNA). Mouse Dmd mRNA was detectable in skeletal and cardiac muscle and at a level approximately 90 percent lower in brain. Dmd mRNA is also present, but at much lower than normal levels, in both the muscle and brain of three different strains of dystrophic mdx mice. The identification of Dmd mRNA in brain raises the possibility of a relation between human Duchenne muscular dystrophy (DMD) gene expression and the mental retardation found in some DMD cases. These results also provide evidence that the mdx mutations are allelic variants of mouse Dmd gene mutations.

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14/7/1 (Item 1 from file: 5)

0013230025 BIOSIS Number: 76037517

DELETION AND AMPLIFICATION OF THE HYPO XANTHINE GUANINE PHOSPHO RIBOSYL TRANSFERASE EC-2.4.2.6 LOCUS IN CHINESE HAMSTER CELLS

FUSCOE J C; FENWICK R G JR; LEDBETTER D H; CASKEY C T

DEP. MED., BAYLOR COLL. MED., HOUSTON, TEX. 77030.

MOL CELL BIOL 3 (6). 1983. 1006-1026. CODEN: MCEBD

Language: ENGLISH

Somatic cell selective techniques and hybridization analyses with a cloned complementary DNA probe were used to isolate and identify Chinese hamster cell lines in which the X-linked gene for hypoxanthine-guanine phosphoribosyltransferase (HGPRT) were altered. Two of 19 HGPRT-deficient mutants selected had major DNA deletions affecting the HGPRT locus. Cytogenetic studies revealed that the X chromosome of each deletion mutant had undergone a translocation event, whereas those from the remaining 17 mutants were normal. Phenotypic revertants of the thermosensitive HGPRT mutant RJK526 were isolated, and amplification of the mutant allele was shown to be the predominant mechanism of reversion. Comparisons of restriction enzyme fragments of DNA for deletion vs. amplification strains identified two regions of the Chinese hamster genome that contained homology to the cDNA probe. One was much larger than the 1600-nucleotide mRNA for HGPRT and to be comprised of linked fragments that contained the functional HGPRT gene. The 2nd was neither transcribed nor tightly linked to the functional gene. These initial studies of HGPRT alterations at the level of DNA, thus identified molecular mechanisms of phenotypic variation.

??t s15/7/1-12

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15/7/1 (Item 1 from file: 5)

0018060315 BIOSIS Number: 85037066

REGIONAL LOCALIZATION OF THE MURINE DUCHENNE MUSCULAR DYSTROPHY GENE ON THE MOUSE X CHROMOSOME

CHAMBERLAIN J S; GRANT S C; REEVES A A; MULLINS L J; STEPHENSON D A; NEFFMAN E P; MONACO A P; KUNKEL L M; CASKEY C T; CHAPMAN V M

INST. MOLE. GENET., BAYLOR COLL. MED., ONE BAYLOR PLAZA, HOUSTON, TEX. 77030.

SOMATIC CELL MOL GENET 10 (6). 1987. 671-673. CODEN: SCMGD

Language: ENGLISH

The murine locus corresponding to the human Duchenne/Becker muscular dystrophy (DMD) gene has been regionally mapped on the mouse X chromosome

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by hybridizing DNA from 12 interspecies mouse crosses with a cDNA clone for the mouse Dmd gene. The results demonstrate that the relative organization of genes on the mouse and human X chromosomes is more divergent than has previously been postulated. Furthermore, the mouse Dmd gene maps to a similar region of the Y chromosome as does the mouse muscular dystrophy mutation mdx, providing further evidence that the mdx mutant may be a murine equivalent of human DMD. However, Southern analysis of portions of the mouse Dmd gene has not yet revealed any differences between mdx and wild-type mice.

15/7/2 (Item 2 from file: 5)

001701161 BIOSIS Number: 84043692

ISOLATION OF COMPLEMENTARY DNA CLONES FOR THE CATALYTIC GAMMA SUBUNIT OF MOUSE MUSCLE PHOSPHORYLASE KINASE: EXPRESSION OF MESSENGER RNA IN NORMAL AND MUTANT MICE

CHAMBERLAIN J S; VANTUINEN P; REEVES A A; PHILIP B A; CASKEY C T
INST. MOLE. GENET., TAYLOR COLL. MED., HOUSTON, TEX. 77030, USA.

PROC NATL ACAD SCI U S A 84 (9), 1987. 2886-2890. CODEN: PNASA

Language: ENGLISH

We have isolated and characterized cDNA clones for the .gamma. subunit of mouse muscle phosphorylase kinase (.gamma.-Phk). These clones were isolated from a .lambda.gt11 mouse muscle cDNA library via screening with a synthetic oligonucleotide probe corresponding to a portion of the rabbit .gamma.-Phk amino acid sequence. The .gamma.-Phk cDNA clones code for a 337-amino acid protein that shares 93% amino acid sequence identity with the corresponding rabbit amino acid sequence. RNA gel blot analysis reveals that the muscle .gamma.-Phk probe hybridizes to two mRNA species (2.4 and 1.6 kilobases) in skeletal muscle, cardiac muscle, and brain, but does not hybridize to liver RNA. Phk-deficient I-strain (Phk) mouse muscle contains reduced levels of .gamma.-Phk mRNA as compared with control mice. Although the Phk defect is an X-linked recessive trait, hybridization to a human-rodent somatic cell hybrid mapping panel shows that the .gamma.-Phk gene is not located on the X chromosome. Rather, the .gamma.-Phk cross-hybridizing human restriction fragments map to human chromosomes 7 (multiple) and 11 (single). Reduced .gamma.-Phk mRNA in I-strain mice, therefore, appears to be a consequence of the Phk-mutant trait and does not stem from a mutant .gamma.-subunit gene.

15/7/3 (Item 3 from file: 5)

0016432369 BIOSIS Number: 82042841

THE 5' FLANKING REGION OF THE ORNITHINE TRANSCARBAMYLASE GENE CONTAINS DNA SEQUENCES REGULATING TISSUE-SPECIFIC EXPRESSION

VERES G; CRAIGEN W J; CASKEY C T
HUNGARIAN ACADEM. SCI., BIOL. RES. CENT., 6701 SZEGED P.O. BOX 521,
HUNGARY.

J BIOL CHEM 261 (17), 1986. 7528-7531. CODEN: JBCHA

Language: ENGLISH

Ornithine transcarbamylase (OTCase) is a mitochondrial matrix enzyme that catalyzes the 2nd step in the mammalian urea cycle. The gene encoding OTCase is located on the X chromosome and expression of OTCase is limited almost exclusively to hepatocytes. We have characterized a .lambda. phage recombinant, isolated from a mouse genomic library, that spans the first two exons of the mouse OTCase gene. Nuclease SI mapping and primer extension analysis of this clone allowed us to determine that the transcription start site is 136 base pairs (bp) upstream from the translation initiation codon. Two TATA-like sequences were found 25 and 153 bp from the transcription initiation point. An 800-bp fragment containing the 5' flanking region of the OTCase gene was fused upstream to the coding sequence of the chloramphenicol acetyltransferase gene to assay promoter activity. This plasmid was introduced into mouse fibroblast NIH 3T3 cells and human hepatoma Hep G2 cells by the calcium phosphate co-precipitation method. After DNA transfection chloramphenicol acetyltransferase activity was observed only in Hep G2 cells. We conclude that this 800-bp fragment contains sufficient information to control OTCase gene expression in a tissue-specific manner, probably by interacting with t. ins-acting factor(s) which are absent in the other cell line.

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1970-71 1971-72 1972-73 1973-74

ORGANIZATION OF THE HUMAN MITOCHONDRIAL POLY(ADP-RIBOSE) TRANSFERASE GENE AND RELATED GENOMES IN THE HUMAN GENOME

DATE: 6-2-1988 APPROVED: 6-2-1988
PATER: R. J. MURDOCH D. J. FRANCIS D. G. LEPPERTED R. H. CASKEY C. T. CUTRIGHT

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EDWARD MIGGIO, M.D., 1401, PAYLESS CELL. OF MED., HOUSTON, TEX. 77030
SENATORIAL, MS. GENET. 16 JULY 1964 AGO AGA BORCH, GOMOR

1100-1101

Using this strategy, synthesis of complementary cDNA probes to DNA from cells carrying either 1 or 2 X chromosomes was used to distinguish sequences derived from the functional locus for hypoxanthine-guanine phosphoribosyltransferase (HPRT) on the X chromosome from 4 independent HPRT-like autosomal sequences in the human genome. Subfragments of cDNA were then used to orient fragments from the HPRT locus with respect to the cDNA sequence. The chromosomal origin of each of the autosomal sequences was determined by Southern analysis using DNA from a panel of human-Chinese hamster somatic cell hybrids. Two of the HPRT-like sequences were localized to chromosome 11, one to chromosome 2, and the 4th to the region between p13 and q11 on chromosome 5. Three of these 4 autosomal sequences were isolated from genomic recombinant libraries and subcloned fragments from each were then used as probes to study restriction fragment length polymorphisms (RFLP) at these loci. A RFLP for *Msp*I was found at the HPRT-like locus on chromosome 5 with a 1.8 kb kilobase major allele (frequency = 0.8) and a 2.4 kb minor allele (frequency = 0.2).

15/7/2013 13:15:56 10.10.10.153

ANALYSIS OF VARIATION AS A MECHANISM FOR DIVERSIFICATION OF AN HABITAT

THE INFLUENCE OF THE CULTURE OF THE PARENT ON THE REACTION OF THE CHILD

ENVIRONMENTAL POLICY

PCR PROTOCOL, 20 MINUTE CYCLE, 40 CYCLES, NOVA SCOTIA, CANADA B3H 4H7.
CONTRACT #111-100-0007 10 JULY 1994. 71-24. SCREEN: SCYD8
100% SPONTANEOUS

Spontaneous DNA was used for hypoxanthine-guanine phosphoribosyltransferase (HGPRT) to analyze the HGPRT gene and mRNA in an HGPRT deficient mutant of Chinese Hamster cells (RJK10) and its HGPRT positive revertants. By Southern blot analysis, no DNA rearrangements were detected within the genes from any of the cell lines examined. Four of 5 spontaneous revertants each contained 10- to 20-fold more copies of the HGPRT gene than did RJK10 or wild-type cells. The gene was not amplified in 4 ultragen-induced revertants. The RJK10 mutation did not alter the size or concentration of HGPRT mRNA and representatives of the revertants contained the mRNA in amounts proportional to the number of genes they carried. Examples of clones with either stable or unstable gene amplification were identified and their HGPRT-positive phenotypes were shown to be dependent on the gene amplification. In a stable revertant, the extra genes were found to be syntetic with the glucose-6-phosphate dehydrogenase. In an unstable revertant only one of the 10-20 copies of the gene could be shown to be "linked" to the HGPRT gene revert by at least 2 distinct mechanisms. A 100% of the HGPRT gene, which occurred spontaneously, or a 100% of the HGPRT gene revert by at least 2 distinct mechanisms.

1576 *Environ Biol Fish* (2007) 80:1567–1576

STRUCTURE EXPRESSION AND MUTATION OF THE HYPX XANTHINE PHOSPHO RIBOSYL TRANSFERASE EC 2.4.2.2 GENE

MELTON, R. H., WONGCHAI, P. S., GREENHORN, J., SACKLEY, G. T.

DEPT. OF MOLECULAR PHYSICS, KING'S BUILD., UNIV. EDINBURGH, EDINBURGH EH9 3JL

PROBLEMS

The guanine hypoxanthine phosphoribosyltransferase (HPRT, EC 2.4.2.8) gene was isolated and its structure was determined. This

gene is > 30 kilobases long and is split into 9 exons. The 5' end of the gene has been determined, and a single-base substitution in the 5' UTR of the cDNA coding sequence from a mouse neuroblastoma cell line that expresses a normal HPRT protein was identified. The 5' end of the gene has been defined, both by nuclease S1 protection and primer extension. The gene has been cultured: this is, was created by ligating the 5' end of the gene to the wild-type human HPRT cDNA. Sequences normally associated with a polyA tail precursors are not present in the immediate 5'-flanking region of the HPRT gene, which is instead highly G+C rich. This observation is discussed in relation to the possible link between DNA methylation and X-chromosome inactivation.

15/7/7 (Item 7 from file: 5)

0014242289 BIOSIS Number: 77075240

A 3 ALLELE RESTRICTION FRAGMENT LENGTH POLYMORPHISM AT THE HYPO XANTHINE PHOSPHO RIBOSYL TRANSFERASE EC-2.4.2.8 LOCUS IN MAN

NUCCIOU R L; CROWDER W E; HOLLOW W L; CASKEY C T

HOWARD HUGHES MED. INSTITUTE LAB., DEP. MED., BAYLOR COLL. MED., HOUSTON, TEX. 77030.

PROC NATL ACAD SCI U S A 80 (13). 1983. 4035-4039. CODEN: PNASA

Language: ENGLISH

Using cloned cDNA complementary DNA1 sequences of murine and human hypoxanthine phosphoribosyltransferase (HPRT; IMP:pyrophosphate phosphoribosyltransferase, EC 2.4.2.8), a 3-allele restriction-fragment-length polymorphism for the restriction endonuclease BamHI at the human HPRT locus is characterized and identified. The alleles are expressed phenotypically on Southern blots as 3 distinct pairs of fragments that hybridize to HPRT cDNA: a 22-kilobase (kb)/25-kb pair; a 12-kb/25-kb pair; and a 22-kb/18-kb pair. In addition to fragments from the HPRT locus, sequences recognized by both HPRT cDNA probes are also present on at least 2 autosomes in the human genome. Allele frequencies in an unselected Caucasian population are 0.77 for the 22-kb/25-kb allele, 0.10 for the 12-kb/25-kb allele, and 0.07 for the 22-kb/18-kb allele, resulting in an average heterozygosity of 38% in females in this population. This polymorphism should facilitate gene mapping by linkage in this region of the human X chromosome.

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15/7/8 (Item 1 from file: 155)

00701035 89000065

Rapid and precise mapping of the Escherichia coli release factor genes by two physical approaches.

Lee CC; Kohara Y; Akiyama K; Smith CL; Craigen WJ; Caskey CT

Institute for Molecular Genetics, Baylor College of Medicine, Houston, Texas 77030.

J. Bacteriol (UNITED STATES) Oct 1989, 170 (10) p4537-41, ISSN 0021-9193 Journal Code: HH3

Contract/Grant No.: GM34436

Language: ENGLISH

The termination of protein synthesis in Escherichia coli requires two codon-specific factors termed RF1 and RF2. RF1 mediates UAA- and UAG-directed termination, while RF2 mediates UAA- and UGA-directed termination. The genes encoding these factors have been isolated and sequenced, and RF2 was found to be encoded in two separate reading frames. The map position of RF1 has been reported as 27 min on the E. coli chromosome, while the RF2 map position has not yet been identified. In this study, two new and independent methods for gene mapping, using pulsed field gel electrophoresis and an ordered bacteriophage library spanning the entire chromosome, were used to localize the map position of the RF2 gene. In addition, the location of the RF1 gene was more precisely defined. The RF2 gene is located at 62.3 min on the chromosome, while the RF1 gene is located at 26.7 min. This approach to mapping cloned genes promises to be a rapid and simple means for determining the gene order of the genome.

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15/7/9 (Item 2 from file: 155)

00701035 89000071

The function, structure and regulation of *E. coli* peptide chain release factors.

Craigie JW, Caskey CT

Hughes Hughes Medical Institute, Baylor College of Medicine, Houston, TX

77030.

Bioch 11 (FRANCE) Oct 1987, 69 (10) p1031-41, ISSN 0300-9004

Journal Code: A14

Contract/Grant No.: GM34480; GM07930

Language: ENGLISH

Document Type: Review

The termination of protein synthesis in *Escherichia coli* depends upon the soluble protein factors RF1 or RF2. RF1 catalyzes UAG and UAA dependent termination, while RF2 catalyzes UGA and UAA dependent termination. The proteins have been purified to homogeneity, their respective genes isolated, and their primary structures deduced from the DNA sequences. The sequences reveal considerable conserved homology, presumably reflecting functional similarities and a common ancestral origin. The RFs are encoded as single copy genes on the bacterial chromosome. RF2 exhibits autogenous regulation in an in vitro translation system. The mechanism of autoregulation appears to be an in-frame UGA stop codon that requires a 1+ frameshift for the continued synthesis of the protein. Frameshifting prior to the inframe stop codon occurs at a remarkably high frequency by an unknown mechanism. Future studies will be directed at understanding how RFs interact with the ribosomal components, and further defining the mechanism of RF2 frameshifting. (43 Refs.)

15/7/10 (Item 3 from file: 155)

05929037 86224037

The 5' flanking region of the ornithine transcarbamylase gene contains DNA sequences regulating tissue-specific expression.

Veres G; Craigie JW; Caskey CT

J Biol Chem Jun 15 1995, 260 (17) p7593-91, ISSN 0021-9252

Journal Code: HIV

Contract/Grant No.: GM07930

Language: ENGLISH

Ornithine transcarbamylase (OTCase) is a mitochondrial matrix enzyme that catalyzes the 2nd step in the mammalian urea cycle. The gene encoding OTCase is located on the X chromosome and expression of OTCase is limited almost exclusively to hepatocytes. We have characterized a lambda phage recombinant, isolated from a mouse genomic library, that spans the first two exons of the mouse OTCase gene. Nuclease SI mapping and primer extension analysis of this clone allowed us to determine that the transcription start site is 136 base pairs (bp) upstream from the translation initiation codon. Two TATA-like sequences were found 25 and 152 bp from the transcription initiation point. An 800-bp fragment containing the 5' flanking region of the OTCase gene was fused upstream to the coding sequence of the chloramphenicol acetyltransferase gene to assay promoter activity. This plasmid was introduced into mouse fibroblast NIH 3T3 cells and human hepatoma Hep G2 cells by the calcium phosphate co-precipitation method. After DNA transfection chloramphenicol acetyltransferase activity was observed only in Hep G2 cells. We conclude that this 800-bp fragment contains sufficient information to control OTCase gene expression in a tissue-specific manner, probably by interacting with trans-acting factor(s) which are not present in the other cell line.

15/7/11 (Item 4 from file: 155)

05269967 84193067

Structure, expression, and mutation of the hypoxanthine phosphoribosyltransferase gene.

Melton BW; Koniecki DS; Brennan J; Caskey CT

Proc Natl Acad Sci U S A Apr 1984, 81 (7) p2147-51, ISSN 0027-8424

Journal Code: PV3

Contract/Grant No.: AM31428-01

Language: ENGLISH

The wild-type mouse hypoxanthine phosphoribosyltransferase (HPRT; IMP:ribonucleotide phosphoribosyltransferase, EC 2.4.2.8) gene has been

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isolated from genomic libraries and its structure has been determined. This X chromosome-linked gene is greater than 33 kilobases long and is split into 11 exons. All the exon sequences have been determined, and a single-base substitution in the HPRT 5' coding sequence from a mouse neuroblastoma cell line that overproduces a mutant HPRT protein has been identified. The 5' end of the gene has been defined, both by nuclease SI protection and primer extension studies and by a functional assay in which an HPRT minigene, capable of expression in cultured cells, was created by ligating the 5' end of the gene onto wild-type human HPRT cDNA. Sequences normally associated with eukaryotic promoters are not present in the immediate 5'-flanking region of the HPRT gene, which is instead highly G+C rich. This observation is discussed in relation to the possible link between DNA methylation and X-chromosome inactivation.

15/7/12 (Item 1 from file # 357)

073736 CBA Accession No.: 83-04585

The genetic structure of mouse ornithine- γ -transcarbamoylase - mapping and DNA sequence determination of ornithine- carbamoyltransferase

AUTHORS: Golde, S E; Verwe G; Caskey C T

CORPORATE SOURCE: Institute for Molecular Genetics, Howard Hughes Medical Institute, Baylor College of Medicine, 1 Baylor Plaza, Houston, TX 77030, USA

JOURNAL: Nucleic Acids Res. (16, 4, 1593-601) CODEN: NARHAD

PUBLICATION YEAR: 1988 LANGUAGE: English

ABSTRACT: The gene encoding the mouse urea cycle enzyme, ornithine- γ -transcarbamoylase (OTC, EC-2.1.3.3, ornithine- carbamoyltransferase) has been isolated and characterized. A mouse genomic DNA library was constructed as a partial λ MaelIII digestion of C57BL/6J mouse DNA cloned into phage Clarm 1A with EcoRI linkers and plated on Y1088 host. Plaque hybridization was performed using a variety of cDNA probes for mouse OTC. Restriction mapping of the clones was carried out using the rapid S-1 nuclease technique, and restriction fragments from phage clone inserts were sequenced by the dideoxy-nucleotide chain termination method after ligation with pUC8 and pUC9 and phage M13 sequencing phage and transformation into competent TG-1 or DH-5- λ phage bacteria. The OTC gene was localized on 5 partially overlapping phage lambda clones. It is split between 10 exons distributed over approximately 70 kb of the X chromosome. The introns are 38 bases to 26 kb in length, while the donor/splice acceptor sequences conform to the consensus of other eukaryotic genes. (27 ref)

?t s23/7/1-23

get

23/7/1 (Item 1 from file # 329)

109001825 CA: 109(11):P25d JOURNAL

Antisense RNA inhibition of endogenous genes

AUTHOR(S): Stout, J. Timothy; Caskey, C. Thomas

LOCATION: Inst. Mol. Genet., Baylor Coll. Med., Houston, TX, 77030, USA

JOURNAL: Methods Enzymol. DATE: 1997 VOLUME: 151 NUMBER: Mol. Genet.

Mamm. Cells PAGES: 510-516 CODEN: MENZAU ISDN: 0076-6879 LANGUAGE:

English

SECTION:

CA203005 Biochemical Genetics

CA214XXX Mammalian Pathological Biochemistry

IDENTIFIER: antisense RNA hypoxanthine phosphoribosyltransferase

deficiency

DESCRIPTION:

Gene and protein structure

Antisense RNA inhibition of endogenous

mRNA levels, mRNA: tRNA: rRNA: complementary...

Antisense RNA inhibition by

RNA PROTEIN HYBRIDES

2010-12-31 Cited by 5, including DNA in modeling of

got

2017-01-01 Cited by 5, including

2002-05-01 Cited by 5, including JOURNAL

2003-01-01 Cited by 5, including sequences of the hypoxanthine-guanine

INST. MOL. GENET., BAYLOR COLL. MED., HOUSTON, TEX. 77030, USA.
11TH INTERNATIONAL SYMPOSIUM ON HUMAN PURINE AND PYRIMIDINE METABOLISM,
KAWASAKI, JAPAN, JULY 17-21, 1988. PEDIATR RES 24 (1). 1988. 124.

2017/7/10

Language: ENGLISH

2017/7/10 (Item 5 from file: 5)

0017051102 BIOSIS Number: 84031232

ORNITHINE TRANSCARBAMYLASE C-TERMINAL STRUCTURE AND THE IDENTIFICATION OF A POINT MUTATION RESPONSIBLE FOR CTC-DEFICIENCY IN THE SPARSE FUR MOUSE

CHAMBERLAIN J S; VERES G; GIBBS R A; CASKEY C T

INST. MOLECULAR GENETICS, BAYLOR COLL. MED., HOUSTON, TEX.

80TH ANNUAL MEETING OF THE AMERICAN SOCIETY OF HUMAN GENETICS, SAN DIEGO, CALIFORNIA, USA, OCTOBER 7-10, 1987. AM J HUM GENET 41 (3 SUPPL.). 1987.

2017/7/10

Language: ENGLISH

2017/7/10 (Item 6 from file: 5)

0017051102 BIOSIS Number: 84031151

ISOLATION OF A COMPLEMENTARY DNA CLONE TO THE MOUSE EQUIVALENT OF THE DUCHENNE MUSCULAR DYSTROPHY GENE

CHAMBERLAIN J S; REEVES A A; MUZNY D M; CASKEY C T

HOWARD HUGHES MED. INST., BAYLOR COLL. MED., HOUSTON, TEX.

80TH ANNUAL MEETING OF THE AMERICAN SOCIETY OF HUMAN GENETICS, SAN DIEGO, CALIFORNIA, USA, OCTOBER 7-10, 1987. AM J HUM GENET 41 (3 SUPPL.). 1987.

2017/7/10

Language: ENGLISH

2017/7/10 (Item 7 from file: 5)

0017051102 BIOSIS Number: 84066479

THE MOLECULAR BASIS OF THE SPARSE FUR MOUSE MUTATION

VERES G; GIBBS R A; SCHERER S E; CASKEY C T

INST. MOLE. GENETICS, HOWARD HUGHES MED. INST., BAYLOR COLL. MED.,

HOUSTON, TEX. 77030.

SCIENCE (WASH D C) 237 (4813). 1987. 415-417. CODEN: SCIEA

Language: ENGLISH

The ornithine transcarbamylase-deficient sparse fur mouse is an excellent model to study the most common human urea cycle disorder. The mutation has been well characterized by both biochemical and enzymological methods, but its exact nature has not been revealed. A single base substitution in the complementary DNA for ornithine transcarbamylase from the sparse fur mouse has been identified by means of a combination of two recently described techniques for rapid mutational analysis. This strategy is simpler than conventional complementary DNA library construction, screening, and sequencing, which has often been used to find a new mutation. The ornithine transcarbamylase gene in the sparse fur mouse contains a C to A transversion that alters a histidine residue to asparagine residue at amino acid 117.

2017/7/10 (Item 8 from file: 5)

0017177757 BIOSIS Number: 83095681

CONSTRUCTION OF A DEFECTIVE RETROVIRUS CONTAINING THE HUMAN HYPOXANTHINE PHOSPHORIBOSYLTRANSFERASE COMPLEMENTARY DNA AND ITS EXPRESSION IN CULTURED CELLS AND MOUSE BONE MARROW

CHANG S M W; WAGER-SMITH K; TSAO T Y; HENKEL-TIGGES J; VAISHNAV S; CASKEY C T

HOWARD HUGHES MED. INST., INST. MOLECULAR GENETICS, BAYLOR COLLEGE MED., HOUSTON, TEXAS 77030.

MOLECUL. BIOL. 7 (2). 1987. 654-663. CODEN: MOBBD

Language: ENGLISH

Defective neurotropic and amphotropic retroviral vectors containing the cDNA for human hypoxanthine phosphoribosyltransferase (HPRT) were developed for efficient gene transfer and high-level cellular expression of HPRT. Helper cell clones which produced a high titer were generated by a simplified method which minimizes cell culture. We used the pZIP-NeoSV(X) vector containing a 5' LTR, 1.5 kb cDNA, 5' poly(A) tail, 100 bp 5'

times, 104/ml) of defective SV40 HPRT B, a vector containing both the hprt and neo genes, were increased 3- to 12-fold by cocultivation of the ecotropic psi.2 and amphotropic PA312 helper cells. Higher viral titers (8 times, 105 to 7.5 times, 106) were obtained when nonproducer NIH 3T3 cells or psi.2 and amphotropic PA312 helper cells. Higher viral titers (8 times, 105 to 7.5 times, 106) were obtained when nonproducer NIH 3T3 cells or psi.2 cells carrying a single copy of SV40 HPRT B were either transinfected or infected by Moloney leukemia virus. The SV40 HPRT B defective virus partially corrected the HPRT deficiency (4 to 50% of normal) of cultured rodent and human Leish-Meyan cells. However, instability of HPRT expression was detected in several infected clones. In these unstable variants, both retention and loss of the SV40 HPRT B sequences were observed. In the former category, cells which became HPRT- (6-thioguanine resistant EC931) also became G418s, indicative of a cis-acting down regulation of expression. Both hypoxanthine-aminopterin-thymidine resistance (HATR) and G418s could be regained by counterselection in hypoxanthine-aminopterin-thymidine. In vitro mouse bone marrow experiments indicated low-level expression of the hprt gene in in vitro CFU assays. Individual CFU were isolated and pooled, and the human hprt gene was shown to be expressed. These studies demonstrated the applicability of vectors like SV40 HPRT B for high-titer production of defective retroviruses required for hematopoietic gene transfer and expression.

23/7/11 (Item 9 from file 5)

0016643192 DIALOG Number: 3100/300

5' REGULATORY ELEMENTS OF THE HUMAN HYPOXANTHINE PHOSPHORIBOSYLTRANSFERASE GENE

PATEL P J, TRACO T, CASHKEY C T, CHINAULT A C
BAYLOR COLL. OF MED., HOUSTON, TX 77030.

SYMPOSIUM ON TRANSCRIPTIONAL CONTROL MECHANISMS HELD AT THE 15TH ANNUAL MEETING OF THE UCLA (UNIVERSITY OF CALIFORNIA-LOS ANGELES) SYMPOSIA ON MOLECULAR AND CELLULAR BIOLOGY, APR. 6-10, 1986. J CELL BIOCHEM SUPPL 0 (10 PART 2), 1986, 173. CODEN: JCDBB

Language: ENGLISH

23/7/12 (Item 10 from file 5)

0011101557 DIALOG Number: 81091970

FINE STRUCTURE OF THE HUMAN HYPOXANTHINE PHOSPHORIBOSYLTRANSFERASE GENE

PATEL P J, TRACOON P C, CASHKEY C T, CHINAULT A C
DEP. BIOCHEMISTRY, BAYLOR COLLEGE MED., HOUSTON, TEXAS 77030.
MOL CELL BIOL 4 (2), 1981, 393-403. CODEN: MCBBD

Language: ENGLISH

The human hypoxanthine phosphoribosyltransferase (HPRT) gene has been characterized by molecular cloning, mapping, and DNA sequencing techniques. The entire gene, which is about 44 kilobases in length, is composed of nine exon elements. The positions of the introns within the coding sequence are identical to those of the previously characterized mouse HPRT gene, although there are significant differences between intron sizes for the two genes. HPRT minigenes have been used in a transient expression assay involving microinjection ATG codon. The promoter of this gene resembles those of other recently characterized "housekeeping" genes in that it lacks CAAT- and TATA-like sequences, but contains several copies of the sequence CGCGCG. Both RNase protection and primer extension analysis indicate that human HPRT RNA is heterogeneous at the 5' terminus, with transcription initiation occurring at sites located \sim 104 to \sim 169 base pairs upstream of the ATG codon. Comparison of the mouse and human HPRT 5' flanking regions indicates that there are only limited stretches of conservation, although there are other shared features, such as an "ATG" family of potential methylation sites, that may have functional significance.

23/7/12 (Item 11 from file 5)

0011101557 DIALOG Number: 80939913

EXPRESSION OF HUMAN AND XENIC HYPOXANTHINE PHOSPHORIBOSYLTRANSFERASE

1986

TRACO T M, TRACOON P C, PATEL P J, CHINAULT A C, MELTON D M, CASHKEY C T

JOHNSON HENRIKSEN, JR., TAYLOR COLLEGE MED., HOUSTON, TX.
ET AL. INTERNATIONAL CONFERENCE ON HYPOXANTHINE-GUANINE PHOSPHORIBOSYL TRANSFERASE DEFICIENCY, SAN DIEGO, CALIF., USA, MAY 20 AND 21, 1985. PEDIATRIC PEG 19 (7). 1985.
749. COHEN, PETER
Language: ENGLISH

~~CONFIDENTIAL~~

22/7/14 (Item 12 from 41465:5)

0314266762 BICBIC N. L. 1 7205130242

HUMAN HYPO XANTHINE GUANINE PHOSPHORIBOSYL TRANSFERASE DEFICIENCY OF A MUTANT allele BY RESTRICTION ENZYME ANALYSIS

WILSON, J. M.; FREDRICKSON, P.; HUGOONAKH, D. L.; CASKEY, C. T.; KELLEY, W. N.
SER. INSTITUTION MED., UNIV. MICHIGAN MED. SCH., ANN ARBOR, MICH. 48109.
J CLIN INVEST 70 (2), 1993 767-770. CODEN: JCIMA

Language: ENGLISH

A sensitive and rapid method for the direct analysis of a hypoxanthine-guanine phosphoribosyl transferase (HPRT) allele associated with a deficiency of enzyme activity and an early onset of gout. The functionally abnormal allele, called the "Toronto" allele (HPRT-Toronto) differs from the normal allele by a single amino-acid-glycine substitution at position 50. A single amino-acid change in the codon for arginine 50 can explain this difference. Direct analysis of this point mutation is based on the restriction endonuclease recognition site in HPRT DNA. As previously reported, DNA from fibroblast individuals with the HPRT-Toronto allele exhibits an abnormal cleavage pattern when digested with Taq I and Kpn I. The HPRT complementary DNA is a 4.0/2.0-kilobase fragment is replaced by a 4.0-kb fragment. The 4.0/2.0-kb restriction fragment was used to detect the HPRT-Toronto allele in a heterozygote that was 50% normal. This approach to the classical techniques used to diagnose hypoxanthine-guanine phosphoribosyl transferase deficiency.

~~CONFIDENTIAL~~

22/7/14 (Item 13 from 41465:5)

0314266763 BICBIC N. L. 1 7205130274

CLONED COMPLEMENTARY DNA SEQUENCES OF THE HYPO XANTHINE GUANINE PHOSPHORIBOSYL TRANSFERASE GENE FROM A MOUSE NEUROBLASTOMA CELL LINE FOUND TO HAVE AMPLIFIED GENOMIC SEQUENCES

BRENNAND, J.; CHINUAULT, A. C.; KONECKI, D. S.; MELTON, D. W.; CASKEY, C. T.
REHARD HUGHES MED. INST. LAB., TAYLOR COLL. MED., HOUSTON, TEX. 77030.
J BIOI NATL ACAD SCI U S A 79 (6). 1982. 1950-1954. CODEN: PNASA

Language: ENGLISH

Cloned complementary DNA sequences of the murine hypoxanthine/guanine phosphoribosyltransferase (HPRT; EC 2.4.2.3) gene were isolated by using a mouse neuroblastoma cell line containing increased levels of a variant HPRT protein. These sequences were used as probes to demonstrate that protein over-production in this cell line is a consequence of at least a 20-fold increase in HPRT mRNA levels resulting from approximately 50-fold amplification of HPRT genomic sequences. The largest cDNA insert so far characterized may code about 70% of the HPRT mRNA sequence. This cDNA possesses 75% of homology with mRNA and DNA from Chinese hamster, bovine, and human. This facilitating detailed analysis of this locus in Mouse 4 sy.

~~CONFIDENTIAL~~

22/7/14 (Item 14 from 41465:5)

0314266764 BICBIC N. L. 1 7205130285

STRUCTURAL ANALYSIS OF MUTANT AND REVERTANT FORMS OF CHINESE HAMSTER HYPO XANTHINE GUANINE PHOSPHORIBOSYL TRANSFERASE EC-2.4.2.6

YUAN, D. B.; FENNICK, P. C. JR.; CASKEY, C. T.
TAYLOR HUGHES MED. INST., HOUSTON, TEX. 77030.
J BIOL CHEM 256 (14). 1981. 2030-2031. CODEN: JBCMA

Language: ENGLISH

Two cell lines of Chinese hamster cells that were selected for hypoxanthine-guanine phosphoribosyl transferase activity following treatment of wild type cells with 6-thioguanine or 6-thioguanine, respectively. The cell lines were found to have a defect in the biosynthesis of hypoxanthine-guanine phosphoribosyl transferase (EC 2.4.2.6) that was either inactive, in the case of RJK2, or had altered, definitely binding properties in the case of RJK3. The sites of defect in RJK2 and RJK3 was not clear, increased mobility of

the column, followed by 0.05M sodium chloride-polyacrylamide gel electrophoresis of samples. **Best Available Copy** peptides of hypoxanthine-guanine phosphoribosyltransferase from wild type, RJK3, RJK39 and revertant of RJK39 were analyzed by high pressure cation exchange chromatography. The RJK39 enzyme is composed of a minimum of 10 lysine- and 12 arginine-containing tryptic peptides. A methionine-containing peptide, which is not found in the carboxy-terminal tryptic peptide based upon the RJK39 sequence, is also exhibited resistance to carboxypeptidase B. The carboxy-terminal peptides of the RJK3 and RJK39 enzymes each differed from the wild type protein in 1 amino acid residue, resulting from the wild type protein in 1 amino acid deletion. The RJK39 terminal tryptic peptides of the RJK3 and RJK39 enzymes are identical, eliminating the possibility that either a frameshift or a missense mutation is the cause of the methionine. The lysine-containing peptide, which is not found in the analysis of the RJK39 enzyme, is also not found in the peptides obtained from the enzymes produced by 3 other mutants. These results strongly implies a nonsense or deletion mutation in the RJK39 codon 112, which is located in the structural gene for hypoxanthine-guanine phosphoribosyltransferase.

22/7/19 13:11:51

SEARCHED BISCOM 11/1/1995

SEARCHED MEDLINE 11/1/1995
SEARCHED EMBASE 11/1/1995
SEARCHED CINAHL 11/1/1995
SEARCHED LILACS 11/1/1995

SEARCHED NURSING & ALLIED HEALTH CARE 11/1/1995
SEARCHED CDSR 11/1/1995
SEARCHED CCR 11/1/1995
SEARCHED EBM 11/1/1995

SEARCHED HUGHES LAB. STUDY GENET. BISCOM, DEP. MED., BAYLOR COLL. MED.,

HUSTON, TEX. 77030, USA.

SEARCHED 12 (2). 1977 389-391. CODEN CELD

Language: ENGLISH

Chinese hamster cells selected for resistance to 9-azaguanine following mutagenesis harbored an active guanine phosphoribosyltransferase (GPT; EC 2.4.2.1) with characteristics compatible with different mutations in the structural gene for that enzyme. Using immunopurification and SDS-sodium dodecyl sulfate-polyacrylamide gel electrophoresis, mutants producing enzyme with altered forms of the enzyme can be analyzed for changes in the MW of GPT. Enzymes from variant clone mutants RJK3 and RJK39 are reduced in MW to 55% and 72%, respectively. GPT activity is not detectable in RJK39. The enzyme from RJK3 is active but has altered characteristics. RJK3, RJK39 and RJK37, have normal MW. The genetic analysis of RJK39 and 37 are probably missense mutations, while RJK3 and RJK37 contain deletions or mutations causing premature peptide chain termination. Cell hybridization between RJK39 and a revertant of that clone with GPT of normal MW revealed that the revertant probably arose by a chromosomal deletion rather than extragenic mutation or suppression.

22/7/19 13:11:51 from file: 155)

22/7/19 13:11:51

The Chinese hamster system in molecular genetics.

W.M. C. O'LEARY, CT

Department of Human Genetics, University of Utah School of Medicine, Salt Lake City 84132.

Sci. 11. Jun 12 1988, 240 (4856) p1493-6, ISSN 0036-8075

11. 11. 1995 13:11:51

Lang. Eng. ENGLISH

Document Type: Review

The Chinese hamster system for choosing to develop the human as the major model experimental system in genetics: an obvious social context that has interested, wide medical observation of the population that provides identification of an abundance of genetic defects, and our ability to produce in the human subtle or complex variations that may not be achievable in other species. Various lines of genetic inquiry that are based on research in other systems—cytogenetic analysis, biochemical studies, mapping of defective loci by linkage analysis in affected families, and other techniques such as the creation of transgenic

organisms complement and enrich each other. New phenomena that could not have been predicted from investigations in other organisms have been found in the last 5 years. The discovery of the "giant" Duchenne muscular dystrophy gene and the identification of recessive cancer genes. Genetic research is yielding insights into human biology that are raising new possibilities for therapy and prevention of disease, as well as challenges to society in the form of ethical decisions about the appropriate application of genetic information. (60 Refs.)

23/7/19 (Item 2 from file: 155)

01229407 87212407

The molecular basis of the sparse fur mouse mutation.

Wu J, Pillek RA, Gruber SE, Caskey CT
Science Jul 24 1987, 237 (4810): p415-7, ISSN 0036-8075

Journal Code: 1137

Contract/Grant No.: HD21452

Language: ENGLISH

The ornithine transcarbamylase-deficient sparse fur mouse is an excellent model to study the most common human urea cycle disorder. The mutation has been well characterized by both biochemical and enzymological methods, but the exact nature has not been revealed. A single base substitution in the complementary DNA for ornithine transcarbamylase from the sparse fur mouse has been identified by means of a combination of two recently described techniques for rapid mutational analysis. This strategy is simpler than conventional complementary DNA library construction, screening, and sequencing, which has often been used to find a new mutation. The ornithine transcarbamylase gene in the sparse fur mouse contains a C to A transversion that alters a histidine residue to an asparagine residue at amino acid 117.

X

23/7/20 (Item 3 from file: 155)

01090022 87064322

Fine structure of the human hypoxanthine phosphoribosyltransferase gene.

Patel PI; Franson PE; Caskey CT; Chinnault AC
Mol Cell Biol Feb 1983, 6 (2): 393-400, ISSN 0270-7306

Journal Code: NCY

Contract/Grant No.: AM31428

Language: ENGLISH

The human hypoxanthine phosphoribosyltransferase (HPRT) gene has been characterized by molecular cloning, mapping, and DNA sequencing techniques. The entire gene, which is about 44 kilobases in length, is composed of nine exon elements. The positions of the introns within the coding sequence are identical to those of the previously-characterized mouse HPRT gene, although there are significant differences between intron sizes for the two genes. HPRT minigenes have been used in a transient expression assay involving microinjection into HPRT- cells to demonstrate functional promoter activity within a 234-base-pair region upstream from the ATG codon. The promoter of this gene resembles those of other recently characterized "housekeeping" genes in that it lacks CAAT- and TATA-like sequences, but contains several copies of the sequence GGGGG. Both RNase protection and primer extension analysis indicate that human HPRT mRNA is heterogeneous at the 5' terminus, with transcription initiation occurring at sites located 300 to 1,100 base pairs upstream from the ATG codon. Comparison of the mouse and human HPRT 5'-flanking sequences indicates that there are only limited stretches of conserved sequence, although there are other shared features, such as an extremely high density of potential methylation sites, that may have functional significance.

Jep X

23/7/21 (Item 4 from file: 155)

05710047 81014347

Expression of human HPRT-4 in the central nervous system of transgenic mice.

Stout JT; Chen W; Brodhead J; Caskey CT; Carter RL
Nature Sep 10-17 1986, 317 (6034): 250-2, ISSN 0028-0836

Journal Code: 1137

Contract/Grant No.: AM 31428; NC 17321

Languages: ENGLISH

Severe deficiency of hypoxanthine-guanine phosphoribosyltransferase (HPRT) in man results in the Lesch-Nyhan syndrome, an X-linked neurological disorder characterized by mental retardation, choreoathetosis and a compulsive tendency toward self-mutilation. Although the HPRT gene is normally constitutively expressed in all tissues at low levels, expression is elevated approximately 100-fold in several regions of the central nervous system, particularly in the basal ganglia. The relationships between HPRT deficiency, the specific alterations of nucleotide metabolism and the neuropathology of the Lesch-Nyhan syndrome remain unclear. Here we have created recombinant molecules containing human HPRT (hHPRT) complementary RNA, the mouse metallothionein-I (MT-I) promoter and the 5' 3' unspliced portion of the human growth hormone (hGH) gene into mouse embryos. We produced transgenic animals that express hHPRT on induction by cadmium. The hHPRT cDNA in these experiments contained 98 base pairs (bp) of 5'-untranslated and 180 bp of 3'-untranslated sequences, and the full-length coding sequence. We studied the in vivo expression of this MT-hHPRT fusion gene and observed preferential hHPRT expression in tissues of the central nervous system (CNS). This study suggests that sequences within the hHPRT transcript (cDNA) influence CNS expression via increased synthesis or stability of messenger RNA.

20/7/22 (Item 5 from file: 155)

14057007 82090407

Hypoxanthine-guanine phosphoribosyltransferase genes of mouse and Chinese hamster: construction and sequence analysis of cDNA recombinants.

Monacki DS; Brennaud J; Fuscoe JC; Caskey CT; Chinault AC

Nucleic Acids Res Nov 11 1982, 10 (21) p6763-75, ISSN 0301-5610

Journal Code: CR1

Contract/Grant No.: GM07526

Languages: ENGLISH

Recombinant plasmids containing DNA inserts complementary to mRNA coding for hypoxanthine-guanine phosphoribosyltransferase (HPRT) from mouse and Chinese hamster cell lines have been isolated from cDNA libraries and characterized by DNA sequence analysis. A total of 1292 nucleotides of the mouse cDNA sequence and 1301 nucleotides of the Chinese hamster cDNA sequence has been determined. Each of these sequences includes an open reading frame of 654 nucleotides (218 amino acids) corresponding to the HPRT protein coding region. The deduced amino acid sequences for the mouse and Chinese hamster enzymes are presented and compared to that of human HPRT. At least 95% of the amino acids are conserved in the three species. In addition, we present evidence that two species of HPRT mRNA, which differ in the site of polyadenylation that is utilized during processing of the RNA transcripts, exist in Chinese hamster cells.

20/7/23 (Item 6 from file: 155)

02089408 70022403

Forward and reverse mutations affecting the kinetics and apparent molecular weight of mammalian HGPRT.

Fenwick RS Jr; Sawyer TH; Kruh GD; Astrin KH; Caskey CT

Cell Oct 1977, 12 (2) p283-91, ISSN 0022-6674 Journal Code: CR4

Languages: ENGLISH

Chinese hamster cells selected for resistance to 9-azaguanine following mutagenesis have hypoxanthine-guanine phosphoribosyltransferase (HGPRT; E.C. 2.4.2.9) with characteristics compatible with different mutations in the structural gene for that enzyme. Using immunopurification and SDS-polyacrylamide electrophoresis, mutants producing antigenically active forms of the enzyme can be analyzed for changes in the molecular weight of HGPRT. Enzyme subunits from mutants R4K3 and R4K3P are reduced in molecular weight by an estimated 4 and 2%, respectively. HGPRT activity is not detectable in R4K2P. The enzyme from R4K3 is active but has altered substrate binding properties. Enzymes from two other mutants with altered kinetic properties, R4K4 and R4K7, have normal molecular weights. The genetic alterations of R4K4 and 47 are probably missense mutations, while R4K2 and 49 could contain either deletions or mutations causing premature

peptides. In contrast, genetic cell hybridization between RUM39 and a descendant of that strain, and SDS-PAGE of muscle molecular weight revealed that the mutation, initially cause by intragenic mutation rather than extragenic mutation (Lyon et al., 1982).

21/22/7/1-2

32/7/1 (Item 1 from file: 5)

001010103 BIBSYS Number: 07092617

EVIDENCE AGAINST LOCATION OF THE GENE FOR FACIOSCAPULOHUMERAL MUSCULAR DYSTROPHY ON THE DISTAL LONG ARM OF CHROMOSOME 14

LENT P W; MEADES J G; UMAPATIKA M; SARTARAZI M; HARPER P S
DEP. MED. GENETICS, ST. MARY'S HOSP., WHITWORTH PARK, MANCHESTER M13 0JH, UK.

J NEUROL SCI 82 (1-3). 1983. 287-292. CODEN: JNSCA

Language: ENGLISH

A panel of 399 individuals from 24 kindreds with facioscapulohumeral muscular dystrophy (FSHD) has been established for genetic linkage studies. A previous suggestion of linkage on the distal long arm of chromosome 14 to the locus (IGM6) for the constant region of the heavy chain of IgG immunoglobulin was tested from serum IgM allotypes and from DNA analysis using an IGM3 DNA probe. After applying an age-dependent weighting for presently unaffected but at-risk individuals close linkage between the IGM6 and FSHD loci was excluded.

X

32/7/2 (Item 2 from file: 5)

001000103 BIBSYS Number: 05010754

AN IMPROVED METHOD FOR PREGNATAL DIAGNOSIS OF GENETIC DISEASES BY ANALYSIS OF AMPLIFIED DNA SEQUENCES: APPLICATION TO HEMOPHILIA A

KOZUM C C; RUBINSTEIN M; GITSCHEIER J
HOWARD HUGHES MED. INST., BOX 0724, UNTV. CALIFORNIA, THIRD PARNASSUS AVE., SAN FRANCISCO, CALIF. 94143.

N ENGL J MED 317 (14). 1987. 885-890. CODEN: NEUMA

Language: ENGLISH

We report the development of a rapid nonradioactive technique for the genetic prediction of human disease and its diagnostic application to hemophilia A. This method is based on enzymatic application of short segments of human genes associated with inherited disorders. A novel feature of the procedure is the use of a heat-stable DNA polymerase, which allow the repeated rounds of DNA polymerase, which allows the repeated sequence of DNA synthesis to proceed at 36 degree C. The high sequence specificity of the amplification reaction of this elevated temperature permits restriction-site polymorphisms, contained in the amplified samples, to be analyzed by visual inspection of their digestion products on polyacrylamide gels. By means of this method, we have performed carrier detection and prenatal diagnosis of hemophilia in two families with use of the factor VIII intragenic polymorphisms identified by the restriction enzymes BclI and KpnI. Predictions can be made directly from chorionic villi, without previous DNA extraction, and fetal sex can be determined by amplification of sequences specific for the Y chromosome. Specific amplification of genomic sequences with heat-stable DNA polymerase is applicable to the diagnosis of a wide variety of inherited disorders. These include diseases diagnosed by restriction-site variation, such as Duchenne's muscular dystrophy and sickle cell anemia, those due to a collection of known mutations, such as beta-thalassemia, and those due to gene deletion, such as alpha-thalassemia.

get

32/7/2 (Item 3 from file: 5)

001455303 BIBSYS Number: 020023298

EXPRESSION OF THE MOUSE HYPOXANTHINE PHOSPHORIBOSYLTRANSFERASE GENE: DELETIONAL ANALYSIS OF THE PROMOTER REGION OF AN X-CHROMOSOME LINKED HAIRLESS GENE

NELSON D W; MOEYAN C; MCKEE A B; REID A M
DEP. MOL. BIO., UNTV. EDINBURGH, MAYFIELD RD., EDINBURGH EH9 3JR, UK.

CELL 44 (2). 1986. 219-229. CODEN: CELLE

Language: ENGLISH

The mouse hairless gene, a mouse hypoxanthine phosphoribosyltransferase gene, like several other

get

housekeeping genes, with many of the features associated with promoters of RNA polymerase II-transcribed genes. mRNA transcripts have multiple initiation sites and a 'PIT' (ridge) was used to show that only 49 bases of 5' flanking sequence was necessary for basal expression in cultured cells. The essential region, which occurs within a complex series of direct repeats is homologous to sequences upstream of other housekeeping genes. When this sequence was deleted, cryptic upstream initiation sites were revealed. Similar element patterns of initiation were seen with all nine genes analyzed in Xba, 1 cells. We speculate that this region of the Hprt promoter is involved in a different interaction with the 'transcriptional' position, to that occurring at more conventional promoters.

32/7/4 (Item 4 from file 5)

001614556 B10812 Number: 00013462

CLONING AND SCREENING WITH NANOMGRAM AMOUNTS OF IMMUNOPURIFIED MESSENGER RNA COMPLEMENTARY DNA CLONING AND CHROMOSOMAL MAPPING OF CYSTATHIONINE BETA SYNTHASE AND THE BETA SUBUNIT OF PROPIONYL COENZYME A CARBOXYLASE

KRAUS J P; WILLIAMSON C L; FIRGAIRA F A; YAN-FENG T L; MUNKE M; FRANKE U; ROSENBERG L E

YALE UNIV. SCH. MED., DEP. HUMAN GENETICS, 300 CEDAR ST., P.O. BOX 3232, NEW HAVEN, CT. 06510.

PROC NATL ACAD SCI U S A 83 (7). 1986. 2047-2051. CODEN: PNASA

Language: ENGLISH

We have developed conditions for efficient cDNA cloning of nanogram amounts of purified mRNAs coding for cystathione β -synthase (L-cysteine hydro-lyase (adding homocysteine), EC 4.2.1.22) and for the cytosolic precursors of mitochondrial ornithine transcarbamylase (carbamoyl-phosphate-L-ornithine carbamoyltransferase, EC 2.1.3.3) and the β -subunit of propionyl-CoA carboxylase [propanoyl-CoA: carbon-dioxide ligase (ADP-forming), EC 6.4.1.31]. The three mRNAs, prepared by sequential immunoselection from the same batch of rat liver polyribosomes, were pooled (20 μ g each), and cDNA was synthesized by using avian reverse transcriptase. The second DNA strand was prepared by "nick-translation repair" of the cDNA construct: mRNA hybrid with RNase H, polymerase I, and DNA ligase from *Escherichia coli*. The double-stranded (ds) DNA was tailed with deoxy-cytidine residues, annealed with Pst I-cut/dG-tailed pBR322, and used to transform *E. coli*. The library generated by this three-step procedure contained 5000 independent colonies. A 550-base-pair (bp) cDNA clone of the β -subunit of propionyl-CoA carboxylase was detected by hybrid-selected translation; it was then used to screen the library for longer cDNAs. Two hybridizing cDNAs, 1200 and 1000 bp long with a 200-bp overlap, representing together a full-length copy of the coding region and 446 bp of 3' untranslated sequence, were recovered. Each plasmid mapped to the region q13.3-q22 of human chromosome 3. Cystathione β -synthase clones were obtained by screening the library with a single-stranded 132PcDNA prepared directly from the highly purified synthase mRNA by reverse transcriptase. The longest hybridizing cDNA of 1700 bp was used in hybrid-selected translation and detected a polypeptide of 63 kDa, identical in size to rat liver synthase. *In situ* hybridization of this cDNA to q22 of human chromosome 3 confirmed the previous tentative assignments of the synthase locus to this chromosome.

32/7/5 (Item 5 from file 5)

001614556 B10812 Number: 00036220

THE HUMAN DNA POLYMERASE ALPHA GENE IS LOCATED ON THE SHORT ARM OF THE X CHROMOSOME

WANG T S-F; REEDSON E F; SUOMALAINEN H A; MOHANDAS T; SHAPIRO L J; SCHRÖDER A; KERN J

STANFORD MED. SCH., STANFORD, CALIF.

EIGHTH INTERNATIONAL WORKSHOP ON HUMAN GENE MAPPING, HELSINKI, FINLAND, AUG. 4-10, 1985. CYTOGENET. CELL GENET. 40 (1-4). 1985. 773. CODEN: 00021B

Language: ENGLISH

32/7/6 (Item 6 from file 5)

001614556 B10812 Number: 00021871

LINKAGE STUDIES IN AUTOSOMAL DOMINANT FACIOSCAPULOHUMERAL MUSCULAR DYSTROPHY
PADERO C; CRIMSTAD M; VOLKERS M G; FERNANI L; VAN LOGHEM E; MEERA KHAN P; NIJMEIJER L E; FRANK J C; SPREIJER G M T
DEP. OF NEUROLOGY, UMCW, HOSPITAL LEIDEN, RIJNSBURGERWEG 10, 2333 AA LEIDEN, THE NETHERLANDS

J NEUROL SCI 15 (2). 1994. 251-263. CODEN: JNSCA

Language: ENGLISH

Linkage studies were undertaken in 120 individuals from 10 kindreds with autosomal dominant facioscapulohumeral muscular dystrophy using 35 different marker genes. No linkage was found. The highest lod score was 1.438 for the IgM chain gene cluster (IGH) at a recombination fraction of 0.2. IgM is located on the long arm of chromosome 14. Based on scores of other marker genes and on a recombination map of chromosome 14, the probability that the gene for facioscapulohumeral muscular dystrophy is located on chromosome 14 is estimated to be approx. 6%.

32/7/7 (Item 7 from file: 5)

201115/070 PHS28 Number: 71024270

IMMUNOGLOBULIN CHAIN AMINO TRANSFERASE DEFICIENCY IN CHINESE HAMSTER CELLS COMPLEMENTED BY 2 INDEPENDENT GENES ON HUMAN CHROMOSOMES 12 AND 19

MAJOLI C L; SHAO T B
BIOCHEMICAL GENETICS SECTION, ROSWELL PARK MEMORIAL INSTITUTE, NEW YORK STATE DEPARTMENT OF HEALTH, BUFFALO, NEW YORK 14263.

SOMATIC CELL GENET 6 (5). 1980. 441-452. CODEN: SCGTD

Language: ENGLISH

Branched-chain aminotransferase (BCT) catalyzes the reversible transamination of the branched-chain α -keto acids to the branched-chain L-amino acids. Since branched-chain L-amino acids (L-isoleucine, L-leucine and L-valine) are essential for cell growth, cells which lack BCT were unable to proliferate in media containing α -keto acids in place of the corresponding L-amino acids. CHW-1102, a Chinese hamster cell line, lacks BCT and does not grow in α -keto acid media. Somatic cell hybrids were made by the fusion of CHW-1102 [Hprt-hypoxanthine-guanine phosphoribosyltransferase-deficient] with several human cell lines and isolated on HAT [hypoxanthine-aminopterin-thymidine] medium. Growth assays of hybrid clones on α -keto acid selection media independent of the HAT selection medium indicated 2 cell hybrid phenotypes: either the hybrid clone, like the parental CHW-1102, could not utilize α -keto acid media or the hybrid could proliferate on all 3 α -keto acid media. The ability of hybrid cells to proliferate on α -keto acid media correlated with the presence of either of 2 human genes which independently complemented the Chinese hamster deficiency. Two human genes, BCT1 assigned to chromosome 12 and BCT2 assigned to chromosome 19, coded for the expression of 2 molecular forms of BCT.

32/7/6 (Item 6 from file: 5)

2010106252 PHS28 Number: 69023248

CHROMOSOMAL LOCATION OF THE GENES FOR HUMAN IMMUNOGLOBULIN HEAVY CHAINS CROCE C M; SHANDER M; MARTINIC J; CICUREL L; D'ANCONA G O; DOLBY T W; KOPROWSKI H

WISTAR INST. NATL. BIOL., 36TH ST. AT SPRUCE, PHILADELPHIA, PA. 19104, USA.

PROC NATL ACAD SCI U S A 76 (7). 1979. 3416-3419. CODEN: PNASA

Language: ENGLISH

Somatic cell hybrids between P3x63Ag8 mouse myeloma cells deficient in hypoxanthine phosphoribosyltransferase (EC 2.4.2.8) and either human peripheral lymphocytes or human lymphoblastoid or myeloma cells were studied for the production of human immunoglobulin [Ig] chains and for the expression of enzyme markers assigned to each of the different human chromosomes. Human chromosome 14 was the only human chromosome present in all independent hybrids producing μ , γ , α , and α human H chains. In 2 of the IgD-dependent hybrids that produced human H chains, chromosome 14 was the only human chromosome present in the hybrid cells. Loss of human chromosome 14 from these hybrids resulted in the concomitant loss of their

ability to produce human Ig H chains. The genes for human Ig H chains are located on human chromosome 14 in non-producing human cells.

32/7/9 (Item 1 from file 155)

9800024 98014034

Linkage analysis of the gene for facioscapulohumeral muscular dystrophy on the distal long arm of chromosome 14.

L. M Rønning; S. Upadhyaya; M. Sanfaresi; Harper PS
Institute of Medical Genetics, University of Wales College of Medicine,
Cardiff, UK

J Hum Genet (NETHERLANDS) Dec 1995, 80 (12) p287-92, ISSN 0022-510X

Journal Code: JHG

Languages: ENGLISH

A panel of 399 individuals from 24 kindreds with facioscapulohumeral muscular dystrophy (FSHD) has been established for genetic linkage studies. A previous suggestion of linkage on the distal long arm of chromosome 14 to the locus (IGHG) for the constant region of the heavy chain of IgG immunoglobulin was tested from serum Gm allotypes and from DNA analysis using an IGHG DNA probe. After applying an age-dependent weighting for presenility (unaffected but at risk) individuals close linkage between the IGHG and FSHD loci was excluded.

32/7/10 (Item 2 from file 155)

98712545 98014034

Linkage studies in facioscapulohumeral muscular dystrophy.

P. Duyng; Klaasen EC; Vinken W; De Lange CG; Wintzen AR
Department of Neurology, State University of Leiden, the Netherlands.
Muscle Nerve (UNITED STATES) Aug 1998, 11 (8) p833-5, ISSN 0148-639X

Journal Code: MNG

Languages: ENGLISH

Possible linkage between the locus for autosomal dominant facioscapulohumeral muscular dystrophy and the locus for the constant region of the heavy chains of the IgG immunoglobulins (Gm) was tested in 1 kindred (23 affected and 18 unaffected sibs) using the polymorphic DNA probe D14S1, which is known to be closely linked with Gm. No linkage between the loci for the disease and the probe was found, and the lod scores suggested that the locus for facioscapulohumeral muscular dystrophy is not situated on the distal part of the long arm of chromosome 14.

32/7/11 (Item 3 from file 155)

98359034 98014034

An improved method for prenatal diagnosis of genetic diseases by analysis of amplified DNA sequences. Application to hemophilia A.

Kegan SC; Doherty M; Gitschier J
Howard Hughes Medical Institute, University of California, San Francisco,
CA 94143.

N Engl J Med Oct 15 1997, 337 (16) p985-90, ISSN 0028-4793

Journal Code: NEM

Languages: ENGLISH

We report the development of a rapid nonradioactive technique for the genetic prediction of human disease and its diagnostic application to hemophilia A. This method is based on enzymatic amplification of short segments of human genes associated with inherited disorders. A novel feature of the procedure is the use of a heat-stable DNA polymerase, which allows the repeated rounds of DNA synthesis to proceed at 63 degrees C. The high sequence specificity of the amplification reaction at this elevated temperature permits restriction-site polymorphisms, contained in the amplified samples, to be analyzed by visual inspection of their digestion products on polyacrylamide gels. By means of this method, we have performed carrier detection and prenatal diagnosis of hemophilia in two families with use of the Factor VIII intragenic polymorphisms identified by the restriction enzymes BpuII and KbaII. Predictions can be made directly from the DNA, without previous DNA extraction, and fetal sex can be determined by amplification of sequences specific for the Y chromosome. Such amplification of genomic sequence with heat-stable DNA polymerase is also able to discriminate for wide variety of inherited disorders.

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These include diseases diagnosed by restriction-site variation, such as Pompe's muscular dystrophy and sickle cell anemia, those due to a deletion of exons mutation, such as beta-thalassemia, and those due to gene deletion, such as alpha-thalassemia.

32/7/12 (Item 4 from file: 155)

00023017 8/024017

The localization of a tRNA102 gene near the 3' OH terminus of a fast myosin heavy chain gene. A comparison between normal and dystrophic chickens.

Lezza BJ; Heywood SM

J Biol Chem Jun 5 1984, 261 (16) p7455-60, ISSN 0021-9258

Journal Code: HV

Contract/Grant No.: HD03016-17

Language: ENGLISH

Two genomic fragments were isolated from a normal and a dystrophic library containing the 3'OH terminus of the fast isoform of myosin heavy chain gene. Restriction map analysis confirmed that the genes were similar. The sequences coding for myosin were defined and shown to be the same in each genomic fragment. However, using a cDNA clone for tRNA102 and two specific oligomers for tRNA102 sequences, we determined that only the genomic fragment from normal chick contained homologous sequences to tRNA102. Dystrophic chick DNA did not contain these regions of homology. In addition, the normal genomic fragment transcribes tRNA102 in vitro via RNA polymerase III while the corresponding fragment of DNA from dystrophic chick was inactive. These results suggest that there are detectable differences between the normal and dystrophic genomes in this regard.

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32/7/13 (Item 5 from file: 155)

000274544 86177544

Cloning and screening with nanogram amounts of immunopurified mRNAs: cDNA cloning and chromosomal mapping of cystathione beta-synthase and the beta subunit of propionyl-CoA carboxylase.

Kraus JP; Williamson CL; Fingair FA; Yang-Feng TL; Munke M; Francke U; Rosenberg LE

Proc Natl Acad Sci U S A Apr 1984, 81 (7) p2047-51, ISSN 0027-8424

Journal Code: PVG

Contract/Grant No.: AM 09527; GM 26105; GM 07439

Language: ENGLISH

We have developed conditions for efficient cDNA cloning of nanogram amounts of purified mRNAs coding for cystathione beta-synthase [L-serine hydro-lyase (adding homocysteine), EC 4.2.1.22] and for the cytosolic precursors of mitochondrial ornithine transcarbamylase (carbamoylphosphate: L-ornithine carbamoyltransferase, EC 2.1.3.3) and the beta subunit of propionyl-CoA carboxylase [propionyl-CoA: carbon-dioxide ligase (ADP-forming), EC 6.4.1.3]. The three mRNAs, prepared by sequential immunoselection from the same batch of rat liver polysomes, were pooled (20 ng each), and cDNA was synthesized by using avian reverse transcriptase. The second DNA strand was prepared by "nick-translation repair" of the cDNA, zDNA hybrid with RNase H, polymerase I, and DNA ligase from Escherichia coli. The double-stranded (ds) DNA was tailed with deoxycytidine residues, annealed with Pst I-cut/dG-tailed pBR322, and used to transform E. coli. The library generated by this three-step procedure contained 5000 independent colonies. A 550-base-pair (bp) cDNA clone of the beta subunit of propionyl-CoA carboxylase was detected by hybrid-selected translation; it was then used to screen the library for longer cDNAs. Two hybridizing cDNAs, 1000 and 1020 bp, long with a 200-bp overlap, representing together a 5.11-5.14^{kb} of the coding region and 446 bp of 3' untranslated sequence, were recovered. Each plasmid mapped to the region q12.3----q22 of human chromosome 3. Cystathione beta-synthase clones were obtained by screening the library with a single-stranded [32P]cDNA prepared directly from the highly purified synthase mRNA by reverse transcriptase. The longest hybridizing cDNA of 1700 bp was used in hybrid-selected translation and detected a polypeptide of 63 kDa, identical in size to rat liver synthase. In situ hybridization of this cDNA to q22 of human chromosome 21 confirmed the chromosomal assignment of the synthase locus to this

X

chromosome.

32/7/14 (Item 6 from file 155)

057907202 01031202

Expression of the mouse MPRT gene: deletion analysis of the promoter region of the X-chromosome-linked hypoxanthine phosphoribosyltransferase gene.

Melton BM; Miller C; McNeil AP; Raff CM

Cell Jan 31 1986, 44 (2) p219-29, ISSN 0021-9290 Journal Code: CMA

Languages: ENGLISH

The mouse hypoxanthine phosphoribosyltransferase gene, like several other housekeeping genes, lacks many of the features associated with promoters of RNA polymerases I and II-coded genes. MPRT transcripts have multiple initiation sites and an MPRT oligonucleotide was used to show that only 49 bases of 5' flanking sequence was necessary for basal expression in cultured cells. This essential region, which occurs within a complex series of direct repeats, is homologous to sequences upstream of other housekeeping genes. When this sequence was deleted, cryptic upstream initiation sites were revealed. Similar aberrant patterns of initiation were seen with all minigenes assayed in Xeroderma pigmentosum. We speculate that this region of the MPRT promoter is involved in a different interaction with the transcriptional machinery to that occurring at more conventional promoters.

32/7/15 (Item 7 from file 155)

05790476 01091474

Human DNA polymerase alpha. Localization for heat-labile mouse DNA polymerase alpha and its gene localization on the X chromosome.

Yanaiwa F; Tanabe H; Miyazawa H; Murakami Y; Hori T; Yamada M

Mol Biol Med Oct 1984, 2 (5) p233-35, ISSN 0735-1213 Journal Code: MBL

Languages: ENGLISH

The chromosomal location of human DNA polymerase alpha gene was determined by studies on somatic cell hybrids between a temperature-sensitive mutant cell line of mouse FM3A cells and normal human lymphocytes or a line of human diploid fibroblasts derived from a patient with the fragile X syndrome. A temperature-sensitive mutant, FT20-M6, a 6-thioguanine-resistant derivative of tsFT20, has heat-labile DNA polymerase alpha. Interspecific cell hybrids between FT20-M6 and human cells grow at the non-permissive temperature, indicating that some human chromosomes can compensate for the temperature-sensitive defect of tsFT20 in mouse-human cell hybrids. Three of these hybrid clones were examined further, and were shown to contain heat-stable DNA polymerase alpha that was neutralized with human DNA polymerase alpha-specific monoclonal antibody. Subcloning and segregation tests of these hybrid clones showed a positive correlation between the expression of human DNA polymerase alpha and the presence of the human X chromosome. Two subclones, however, did not conform to this relationship: they grew at the nonpermissive temperature but not in hypoxanthine/aminopterin/thymidine medium. Detailed examination of the human chromosomes in these subclones revealed that these clones had only one human chromosome, the X chromosome with a terminal deletion of the long arm including the locus of the gene for hypoxanthine phosphoribosyltransferase (EC 2.4.2.6). From these data, the functional DNA polymerase alpha gene was located on the human X chromosome.

32/7/16 (Item 8 from file 155)

05782194 01033194

The mom gene of bacteriophage Mu: a unique regulatory scheme to control a lethal function.

Mahmood R; Seiler P; Wolzyn P; Pfleff E

Gene 1985, 29 (1) p61-70, ISSN 0378-1119 Journal Code: FGP

Languages: ENGLISH

The mom gene of bacteriophage Mu encodes a DNA modification function which converts adenosine to adenosine-5'-monophosphate in a sequence-specific manner. The mom gene itself is subject to a complex regulation: gene expression requires methylation by the *Escherichia coli* Dam methylase of specific sites upstream of the mom promoter and transactivation of the promoter by a Mu protein called p6. The requirement for transactivation can be overcome when

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measurements of the rate of fixation of mutations that do not change the amino acid sequence. The minimum estimate of the rate is greater than the highest previously estimated rates of fixation of neutral mutations calculated for fibrinopeptide A. A new technique, deoxysubstitution sequencing, which should speed determination of the complete mRNA sequences, is described.

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Set	Items	Description
51	580	AU=CASKEY, C? OR AU=CASKEY C?
52	827	AU=CHAMBERLAIN, J? OR AU=CHAMBERLAIN J?
53	666	AU=GIBBS, R? OR AU=GIBBS R?
54	19	AU=RANIER, J? OR AU=RANIER J?
55	13	51 AND 52 AND 53 AND 54
56	9	55 NOT PY=1989
57	1990	51 OR 52 OR 53 OR 54
58	1822	57 NOT PY=1989
59	1813	58 NOT 56
510	134	59 AND (PRIMER? OR POLYMERASE? OR CHAIN OR COMPLEMENT?)
511	190346	CHROMOSOME?
512	0	5 510 AND 511
513	12	510 AND 511
514	1	510 AND DELETION?
515	12	510 NOT 514
516	1127	DEONITHINE(2U)TRANSCARBAMYLASE
517	3788	HYPOXANTHINE(2U)PHOSPHORIBOSYLTRANSFERASE
518	747	STEROID(2U)SULFATASE
519	5PC53	MUSCULAR(2U)DYSTROPHY OR MS
520	64962	518 OR 517 OR 518 OR 519
521	60023	520 NOT PY=1989
522	121	510 NOT (514 OR 515)
523	22	521 AND 522
524	373729	PRIMER? OR POLYMERASE? OR CHAIN OR COMPLEMENT?
525	3	X-LINK?
526	3	205 OR X LINK?
527	0	X-LINK?
528	4	YLINK?
529	1726	YCHROMOSOME?
530	59064	521 NOT (56 OR 514 OR 515 OR 516 OR 520)
531	5	520 AND 524 AND (525 OR 528 OR 529)
532	34	(520 AND 524 AND CHROMOSOME?) OR 531

mom is transcribed from foreign promoters. When cloned into various sites in pBR322, the gene is always found in an orientation where transcription from vector promoters is excluded. The productive orientation is 5' TATA 3' CCAAT. This effect is mediated by the concerted action of the TATA box, CCAAT and the product of gene com (control of mom, previously termed CPE-1) whose coding region overlaps the 5'-coding region of the mom gene. When mom is expressed from its own promoter, internal deletions in com completely abolish expression of the com gene. Fragments lacking the 5' end of com can be cloned downstream of constitutive plasmid pGK-Neo. The com gene product itself is not lethal to the cell. The protein, a polypeptide of 27 kDa, has been visualized on gels. Efficient expression of com from pL requires gene com. A fusion between MS-2 polymerase and com has been generated. The fusion product is made in large amounts, whereas the mom gene product is not overproduced although the gene is present on the same transcriptional unit. (ABSTRACT TRUNCATED AT 250 CHARACTERS)

22/7/17 (Item 9 from file: 155)

15500118 85270506

Assignment of the gene for Human ENO polymerase alpha to the X chromosome.

Wang TS; Pearson DE; Suomalainen HA; Mehandas T; Shapiro LJ; Schroeder J; Kurn M

J. of Natl Acad Sci U S A Aug 1985, 82 (16) p5270-4, ISSN 0027-8424

Journal Code: PNC

Contract/Grant No.: CA-14835

Languages: ENGLISH

We have applied an assay based on a monoclonal antibody that discriminates the activity of human DNA polymerase alpha in rodent-human somatic cell hybrid clones to identify a single genetic locus that is both necessary and sufficient for the expression of DNA polymerase alpha. We have mapped this locus to the short arm of the human X chromosome, near the junction of bands Xp21.3 and Xp22.1, and demonstrated that it is not expressed from an inactive X chromosome.

X

22/7/18 (Item 10 from file: 155)

15500507 85155507

Sequence of the promoter region of the gene for human X-linked 3-phosphoglycerate kinase

Singer-Sam J; Keith DH; Tani K; Simmer RL; Shively L; Lindsay S; Yoshida A; Riggs AD

Gene Dec 1984, 82 (3) p109-17, ISSN 0378-1119 Journal Code: PGP

Languages: ENGLISH

We have determined the sequence of an 812-bp BamHI-EcoRI restriction fragment containing the 5' region of the human gene for PGK (3-phosphoglycerate kinase or ATP:3-phospho-D-glycerate 1-phosphotransferase; EC 2.7.2.3). The fragment contains 450 bp 5' to three start points for transcription (located by primer extension and S1 nuclease mapping), a leader sequence 95-94 bp long, the first exon of gene (65 bp), and part of the first intron. The promoter region is extremely G + C-rich, lacks a TATA box, and has an 8-bp direct repeat. A comparison of the promoter region for PGK with other promoters on the X-chromosome reveals homology with the promoter for Hprt, but not with the operator for factor IX.

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22/7/19 (Item 11 from file: 155)

05416767 85032767

Linkage studies in autosomal dominant facioscapulohumeral muscular dystrophy.

Daalting C; Eriksson AE; Volkers MC; Bernini L; Van Leghem E; Meera Khan P; Huijgen LE; Pronk JC; Schreuder GM

J. Medical Sci Sep 1984, 65 (3) p261-8, ISSN 0022-510X Journal Code: JMS

Languages: ENGLISH

Linkage studies were undertaken in 120 individuals from 10 kindreds with autosomal dominant facioscapulohumeral muscular dystrophy using 35

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different marker genes. No linkage was found. The highest lod score was 1.688 for the immunoglobulin heavy chain gene cluster (IGH) at a recombination fraction of 0.2. IGH is located on the long arm of chromosome 14. Based on scores of other marker genes and on a recombination map of chromosome 14, the probability that the gene for facioscapulohumeral muscular dystrophy is located on chromosome 14 is estimated to be approximately 6%.

01/7/21 (Item 12 from file: 155)

05160411 89037444

Influence of inhibitors of poly(ADP-ribose) polymerase on DNA repair, chromosomal alterations, and mutations.

Natarajan AT; van Zeeland AA; Zwanenburg TS

Int Symp Princess Takamatsu Cancer Res Fund 1993, 13 p227-42,

Journal Code: HMC

Language: ENGLISH

The influence of inhibitors of poly(ADP-ribose) polymerase such as 3-aminobenzamide (3AB) and benzamides (B) on the spontaneously occurring as well as mutagen induced chromosomal aberrations, sister chromatid exchanges (SCEs) and point mutations has been studied. In addition, we have measured the influence of 3AB on DNA repair following treatment with physical and chemical mutagens. Post treatment of X-irradiated mammalian cells with 3AB increases the frequencies of induced chromosomal aberrations by a factor of 2 to 3. Both acentric fragments and exchanges increase indicating that the presence of 3AB slows down the repair of DNA strand breaks (probably DNA double strand breaks), thus making breaks available for interaction with each other to give rise to exchanges. 3AB, when present in the medium containing bromodeoxyuridine(BrdUrd) during two cell cycles, increases the frequencies of SCEs in Chinese hamster ovary cells (CHO) in a concentration dependent manner leading to about a 10-fold increase at 10 mM concentration. Most 3AB induced SCEs occur during the second cell cycle, in which DNA containing bromouridine (BU) is used as template for replication. BU containing DNA appears to be prone to errors during replication. The extent of increase in the frequencies of SCEs by 3AB is correlated with the amount of BU incorporated in the DNA of the cells. The frequencies of spontaneously occurring DNA single strand breaks in cells grown in BrdUrd containing medium are higher than in the cells grown in normal medium and this increase depends on the amount of BU incorporated in the DNA of these cells. We have studied the extent of increase in the frequencies of SCEs due to 1 mM 3AB in several human cell lines, including those derived from patients suffering from genetic diseases such as ataxia telangiectasia (A-T), Fanconi's anemia (FA), and Huntington's chorea. None of these syndromes showed any increased response when compared to normal cells. 3AB, however, increased the frequencies of spontaneously occurring chromosomal aberrations in A-T and FA cells. 3AB does not influence the frequencies of SCEs induced by UV or mitomycin C (MMC) in CHO cells. However, it increases the frequencies of SCEs induced by ethyl methanesulphonate (EMS) and methyl methanesulphonate (MMS). Under the conditions in which 3AB increases the frequencies of spontaneously occurring as well as induced SCEs, it does not increase the frequencies of point mutations in hypoxanthine-guanine phosphoribosyltransferase (HGPRT) locus. 3AB does not influence the amount of repair replication following dimethylsulphate (DMS) treatment of human fibroblasts, or UV irradiated human lymphocytes. (ABSTRACT TRUNCATED AT 400 WORDS)

X

02/7/21 (Item 13 from file: 155)

02904041 80045041

Differential staining and segregation of parental chromosomes in mouse-rabbit hybridomas.

Madras L; Phalente L; Bettin G

Cell Biol Int Rep Sep 1979, 3 (6) p503-14, Journal Code: CBI

Language: ENGLISH

Horst G 32258 fluorescent staining can be coupled with G-banding to identify the chromosomal contribution of each parent in mouse-rabbit hybridomas. A fast and essentially complete segregation of rabbit chromosomes is obtained in these cells. The rabbit X chromosome is

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preferentially maintained in media imposing HGPRT activity for cell growth. Mouse-rabbit hybridomas, some of which secrete rabbit immunoglobulin chains, should be a convenient material for the identification of chromosomes governing rabbit Ig chain synthesis.

82/7/22 (Item 14 from file: 155)

00920395 80034695

Chromosomal location of the genes for human immunoglobulin heavy chains. Gross CM; Shander M; Martinis J; Cicurel L; D'Ancona GG; Delby TW; Koprowski H

Proc Natl Acad Sci U S A Jul 1973, 70 (7) p3415-9, ISSN 0027-8424

Journal Code: PV3

Languages: ENGLISH

We have studied somatic cell hybrids between P3x63Ag8 mouse myeloma cells deficient in hypoxanthine phosphoribosyltransferase (EC 2.4.2.6) and either human peripheral lymphocytes or human lymphoblastoid or myeloma cells for the production of human immunoglobulin chains and for the expression of enzyme markers assigned to each of the different human chromosomes. Human chromosome 14 was the only human chromosome present in all independent hybrids producing mu, gamma, and alpha human heavy chains. In two of the independent hybrids that produced human heavy chains, human chromosome 14 was the only human chromosome present in the hybrid cells. Loss of human chromosome 14 from these hybrids resulted in the concomitant loss of their ability to produce human immunoglobulin heavy chains. In view of these results, we conclude that the genes for human immunoglobulin heavy chains are located on human chromosome 14 in immunoglobulin-producing human cells.

X

82/7/23 (Item 15 from file: 155)

009217903 77119903

Structural and genetic studies on chicken 7S immunoglobulin allotypes. II. Distribution of allotypes on the 7S immunoglobulin of homozygous and heterozygous chickens.

Wakeland EK; Benedict AA; Abplanalp HA

J Immunol Feb 1977, 118 (2) p401-4, ISSN 0022-1767 Journal Code:

IFB

Languages: ENGLISH

We have previously reported that chicken 7S immunoglobulin (Ig) heavy (H) chain allotypes (C9-1 locus) segregate as phenogroups in F2 progeny. Specificity C9-1.1 formed a phenogroup with C9-1.4 in inbred chicken line UCD 2, and a second phenogroup with C9-1.3 in line UCD 3. To determine whether these phenogroups were formed by combinations of specificities on the same, or on separate subclasses of 7S Ig, their distribution on the 7S Ig molecules of birds homozygous for 7S Ig allotypes was analyzed by radioimmunoassay. Anti-C9-1.1 and anti-C9-1.3 alloantisera each bound more than 94% of line UCD 3 1252-7S Ig. Similar results were obtained with alloantisera to C9-1.1 and C9-1.4 WITH 125 I-7S Ig from line UCD 2. These results indicate that both phenogroups were formed by combinations of specificities present on the same H chain. Thus, each phenogroup described, probably is the product of a single structural gene which is responsible for more than 94% of the 7S Ig H chain constant regions. In F hybrids with the genotype C9-1.3, 1.3/C9-1.2, two populations of serum 7S Ig molecules were detected by direct and sequential binding analysis with specific alloantisera. One population of 7S Ig contained specificities C9-1.1 AND C9-1.3, but not C9-1.2; while the second population was exclusively the product of one parental allele. Consistent with a genetic regulatory mechanism involving allelic exclusion, no MG Ig containing allotypes produced by both alleles was detected.

X

82/7/24 (Item 16 from file: 155)

009177122 77079130

Pvr-1, a restriction locus of a type C RNA virus in the feline cellular genome: identification, location, and phenotypic characterization in cat X mouse somatic cell hybrids.

O'Brien SJ

Proc Natl Acad Sci U S A Dec 1976, 73 (12) p4818-22, ISSN 0027-8424

Journal Code: PV3

Languages: ENGLISH

Somatic cell hybrids were constructed between BALB/c-RAG mouse cells and feline lymphoma cells by the hypoxanthine-aminopterin-thymidine selection scheme. RAG cells spontaneously produce an endogenous B-tropic type C virus. Cat-mouse hybrids preferentially segregate feline chromosomes and retain murine chromosomes demonstrable by karyotypic and isozyme analyses. Despite the presence of the complete mouse genome, including the viral genome, virus production was diminished to 1-5% of the levels observed in RAG parents based upon particle-associated RNA-dependent DNA polymerase (reverse transcriptase) activity in the culture fluid. Thirty-seven hybrids made on four different occasions had suppressed virus levels, and no hybrids expressed parental virus levels. Reverse selection experiments on 6-thioguanine demonstrated that a restriction gene, tentatively named Bvr-1, was linked to the feline structural genes for hypoxanthine phosphoribosyltransferase (IMP:pyrophosphate phosphoribosyltransferase; EC 2.4.4.3) and glucose-6-phosphate dehydrogenase (D-glucose-6-phosphate:NADP+ 1-oxidoreductase; EC 1.1.1.49) in cats, probably on the X-chromosome. The genetic mode of action of Bvr-1 is trans dominant in restriction of murine leukemia virus. The restriction locus results in a block late in virus maturation but prior to release, since expression of antigens for viral structural proteins and mature budding particles is apparent on surfaces of restricted hybrid cells but not in high-speed pellets from culture fluid of restricted cells.

32/7/25 (Item 17 from file: 155)

02945495 78128495

Mouse MSV transformed cells resistant to S-azaguanine.

Altaner C; Hladka M

Neoplasia 1975, 22 (6) p579-87, ISSN 0028-2885 Journal Code: NVO

Languages: ENGLISH

Mouse cells transformed by murine sarcoma virus were made resistant to S-azaguanine. Resistant cells and cell clones isolated from them were deficient in hypoxanthine-guanine phosphoribosyl transferase (HGPRT) activity. They did not grow in HATC medium, did not incorporate labeled hypoxanthine, and had negligible HGPRT activity. The resistance was genetically stable. The resistant cells were hyperdiploid and contained telocentric chromosomes only. The resistant cells as well as the progenitor cells were slightly tumorigenic in mice, the plating efficiency in soft agar was very low. The parental cells and aza-G resistant cells produced S-type viral particles having RNA-dependent DNA polymerase activity. The resistance to aza-G did not influence the expression of murine sarcoma virus genome in cells. The resistant cells are suitable for preparation of cell hybrids.

32/7/26 (Item 18 from file: 155)

02911404 74092404

Investigation of the organization of mammalian chromosomes at the DNA sequence level.

Salser W; Bowen S; Browne D; el-Adli F; Fedoreff N; Fry K; Heindell H; Paddock G; Peen R; Wallace B; Whitcombe P

Fed Proc Jan 1976, 35 (1) p28-35, ISSN 0014-9346 Journal Code: EUP

Languages: ENGLISH

New developments in DNA sequencing techniques permit rapid progress in the determination of both repetitive and single-copy mammalian sequences. Three distinct families of highly repetitive satellite DNA's from the kangaroo rat *Dipodomys ordii* have been sequenced. With the MG satellite it was possible to show that the basic repeat sequence and its variants were arranged in a nonrandom order suggesting a hierarchy of repeats. The HS-alpha satellite from *D. ordii* was shown to resemble the guinea pig alpha satellite, a long term evolutionary persistence inconsistent with previous models. Sequences from hemoglobin mRNA were determined using hemoglobin complementary DNA as template for transcription in vitro. Seven of the largest fragments have been assigned to untranslated regions of the mRNA whereas 15 others have been tentatively located within the structural genes. From correlations with sequences from corresponding regions in the human hemoglobin mRNA's we have been able to make the first direct